

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

JOHN, Varghese, et al.

Application No.: 09/594,667

Filed: 06/15/00

For: TETRAPEPTIDE INHIBITORS OF  
β-SECRETASE



)  
)  
) Examiner: Unassigned

)  
) Group No.: Unassigned

RECEIVED

MAR 09 2001

TECH CENTER 1600/2900

Certificate of Mailing (37 C.F.R. § 1.8(a)):

I hereby certify that this correspondence and the documents referred to as attached therein are being deposited with the United States Postal Service with sufficient postage as First Class Mail, in an envelope addressed to: Assistant Commissioner for Patents, Washington, D.C., 20231.

Date: 2/26/01

By: Tracey Horne

Assistant Commissioner for Patents  
Washington, D.C. 20231

INFORMATION DISCLOSURE STATEMENT TRANSMITTAL

Dear Sir:

1. Transmitted herewith is:

- ☒ Information Disclosure Statement
- ☒ PTO Form 1449
- ☒ Copies of publications listed on the PTO Form 1449
- ☐ English translation of foreign language reference(s)
- ☐ No copies of publications listed on the PTO Form 1449 are being provided as this application claims continuation status to application Serial No. \_\_\_\_\_ and copies of the listed publications were provided in the parent application.
- ☒ Copy of foreign examination report
- ☐ English translation of foreign examination report

2. ☒ This Information Disclosure Statement is filed before the later of:
- ☐ three months from the filing date of this national application;
  - ☐ three months from the date of entry of the national stage as set forth in 37 CFR 1.491 in an international application; or
  - ☒ the mailing date of a first office action on the merits.

RECEIVED

MAR 09 2001

In accordance with 37 CFR 1.97(b), no fee is required.

TECH CENTER 1600/2900

3. ☐ This Information Disclosure Statement is filed after the events noted in paragraph 2, but before either:
- ☐ Final action under 37 CFR 1.113, or
  - ☐ Notice of Allowance under 37 CFR 1.311.

In accordance with 37 CFR 1.97© also enclosed is:

- ☐ Fee under 37 CFR 1.17(p) in the amount of \$240.00; or
- ☐ Statement as stated below.

4. ☐ This Information Disclosure Statement is filed before the payment of the issue fee, but after either:
- ☐ Final action under 37 CFR 1.113, or
  - ☐ Notice of Allowance under 37 CFR 1.311.

In accordance with 37 CFR 1.97(d) also enclosed is:

- ☐ Statement as specified in 37 CFR 1.97(e)
- ☐ Petition requesting consideration of the Information Disclosure Statement; and
- ☐ The petition fee set forth in 37 CFR 1.17(I) in the amount of \$130.00.

5. Statement. The undersigned states:

- ☒ Each item of information contained in the Information Disclosure Statement cited herein was cited in a communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing date of this Information Disclosure Statement; or
- ☐ No item of information contained in the Information Disclosure Statement submitted herewith was cited in a communication from a foreign patent office in a counterpart foreign application and, to the knowledge of the undersigned, having made reasonable inquiry, was known to any individual designated in 37 CFR 1.56(c) more than three months prior to the filing date of this Information Disclosure Statement.

6. Fees

- ☐ Check in the amount of \$ \_\_\_\_\_ is attached.  
☐ Please charge Deposit Account No. 01-2707 in the amount of \$240.00.  
☒ No fee is required.  
☐ The Commissioner is hereby authorized to charge any underpayment or credit any overpayment of the following fees associated with this communication to Deposit Account No. 01-2707:  
☐ Any patent application processing fees under 37 CFR 1.17.

Date: 26 FEB 01

Respectfully submitted,

J. Mark Hoch  
SIGNATURE OF PRACTITIONER

J. Mark Hoch

Reg. No. 35,195

(650) 616-5035

Customer No.: 21835

Elan Pharmaceuticals Inc.  
800 Gateway Boulevard  
South San Francisco, CA 94080

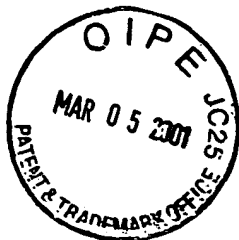
## IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

JOHN, Varghese, et al.

Application No.: 09/594,667

Filed: 06/15/00

For: TETRAPEPTIDE INHIBITORS OF  
β-SECRETASE

) Examiner: Unassigned

) Group No.: Unassigned

RECEIVED

MAR 09 2001

TECH CENTER 1600/2900

## Certificate of Mailing (37 C.F.R. § 1.8(a):

I hereby certify that this correspondence and the documents referred to as attached therein are being deposited with the United States Postal Service with sufficient postage as First Class Mail, in an envelope addressed to: Assistant Commissioner for Patents, Washington, D.C., 20231.

Date: 2/26/01

By: Gracy Horne

Assistant Commissioner for Patents  
Washington, D.C. 20231

INFORMATION DISCLOSURE STATEMENT  
UNDER 37 CFR §1.98 and 37 CFR §1.56

Dear Sir:

Applicant hereby submits this Information Disclosure Statement in accordance with 37 CFR 1.98 and pursuant to Applicant's continuing duty under 37 CFR 1.56 to bring any information which may be material to patentability of this application to the Examiner's attention.

Applicant makes no representation that a search has been conducted by the Applicant, or that there is not possibly more relevant art. Applicant also makes no representation that the information submitted herewith is in fact material.

- ☐ No copies enclosed: The publications listed on the enclosed Form PTO 1449 have been previously cited by or submitted to the PTO as recited in the Information Disclosure Statement Transmittal that accompanies this paper. In accordance with the provisions of 37 CFR 1.98(d), no copies of these publications are being provided.
- ☒ Copies enclosed: Copies of the publications listed on the enclosed Form PTO 1449 are being provided with this Information Disclosure Statement.

- ☒ [X] Some of the enclosed publications were cited in a foreign examination report in a related case. A copy of the search report and the cited references are attached hereto.
- ☐ [ ] The search report is not in the English language and a translation of the search report is enclosed.
- ☐ [ ] At least one of the enclosed publications is not in the English language.
- ☐ [ ] English translation(s) are enclosed.
- ☐ [ ] Enclosed is an explanation of the relevance of non-English publications for which an English translation is not available.
- ☐ [ ] The explanation is in the form of an English language search report.

The subject application is believed patentable over any of the above references.

Date: 26 FEB 01

Respectfully submitted,

  
SIGNATURE OF PRACTITIONER

J. Mark Hoch

Reg. No. 35,195

(650) 616-5035

Customer No.: 21835

Elan Pharmaceuticals Inc.  
800 Gateway Boulevard  
South San Francisco, CA 94080

## INFORMATION DISCLOSURE STATEMENT

(Use several sheets if necessary)



APPLICANT:

Elan Pharmaceuticals, Inc.

FILING DATE

June 15, 2000

GROUP

Unassigned

## U.S. PATENT DOCUMENTS

| *EXAMINER<br>INITIAL | DOCUMENT<br>NUMBER | DATE      | NAME   | CLASS                   | SUBCLASS | FILING DATE |
|----------------------|--------------------|-----------|--------|-------------------------|----------|-------------|
|                      | P1                 | 4,397,786 | 9/1983 | Evans, <i>et al.</i>    |          |             |
|                      | P2                 | 4,522,811 | 6/1985 | Eppstien, <i>et al.</i> |          |             |
|                      | P3                 | 4,636,491 | 1/1987 | Bock, <i>et al.</i>     |          |             |

## OTHER PUBLICATIONS (including Author, Title, Date, Pertinent Pages, Etc.)

|     |  |
|-----|--|
| D1  | Bock, Mark G., <i>et al.</i> "Renin Inhibitors Containing Hydrophilic Groups. Tetrapeptides with Enhanced Aqueous Solubility and Nanomolar Potency" <u>J. Med. Chem.</u> , 31:1918-1923, 1988  |
| D2  | Agarwal, Nirankar S., <i>et al.</i> "Inhibition of Cathepsin D by Substrate Analogues Containing Statine and by Analogues of Pepstatin" <u>J. Med. Chem.</u> , 29:2519-2524  |
| D3  | Bringmann, G., <i>et al.</i> "Enantiomerically Pure N-Boc Protected $\beta$ -Keto- $\gamma$ -Amino Acid Esters form Simple Keto Precursors. A Novel, Stereocontrolled Approach to Statine Derivatives with Any Desired Configuration" <u>Synlett</u> , 5:253-255, 1990 |
| D4  | Cintas, P., "Asymmetric synthesis of $\alpha$ -amino acids from carbohydrates as chiral templates." <u>Tetrahedron</u> , 47(32):6079-6111, 1991  |
| D5  | Fieser, Mary, <i>et al.</i> , <u>Reagents for Org. Syn.</u> , 4:418, 1974  |
| D6  | Freifelder, Morris, <i>et al.</i> , "Low-pressure Hydrogenation of Alkozyanilines with Nobel Metal Catalysts" <u>J. Org. Chem.</u> , 30:2485-6, 1965   |
| D7  | Kessler, Horst, <i>et al.</i> , "Short and Efficient Synthesis of Statine and Isostatine Derivatives" <u>Synthesis</u> , 6:457-458, 1990   |
| D8  | Korotzer, Andrew, <i>et al.</i> "Differential regulation by beta-amyloid peptides of intracellular free $Ca^{2+}$ concentration in cultured rat microglia." <u>Eur. J. Pharmacol.</u> , 288(2):125-130, 1995   |
| D9  | Kowall, Neil, <i>et al.</i> "An <i>in vivo</i> model for the neurodegenerative effects of $\beta$ amyloid and protection by substance" <u>Proc Natl Acad Sci USA</u> , 88(16):7247-7251, 1991  |
| D10 | Lehninger, A.L., <u>Biochemistry: The Molecular Basis of Cell Structure and Function</u> , Chapter 4, Worth Publishers, NY, pp. 71-94, 1975  |
| D11 | Nishi, Takahide, <i>et al.</i> , "The Practical Synthesis of N-Protected Allylamine: The Isoxazoline Route to Statine Analogue" <u>Heterocycles</u> , 29(9):1835-1842, 1989  |
| D12 | Precigoux, G. <i>et al.</i> "X-ray crystallography of linear peptides through renin-angiotensin system." <u>Peptides Biol. Fluids</u> , 35:476-476 (abstract), 1987  |
| D13 | Rich, Daniel, "Pepstatine-Derived Inhibitors of Aspartic Proteinases. A Close Look at an Apparent Transition-State Analogue Inhibitor" <u>J. Med. Chem.</u> , 28(3):263-273, 1985  |
| D14 | Sabbagh, M., <i>et al.</i> " $\beta$ -Amyloid and Treatment Opportunities for Alzheimer's Disease." <u>Alz. Dis. Rev.</u> , 3:1-19, 1997   |
| D15 | Seubert, <i>et al.</i> , "Isolation and quantification of soluble Alzheimer's $\beta$ -peptide from biological fluids" <u>Nature</u> , 359:325-327, 1992   |
| D16 | Shiosaki, K. <i>et al.</i> "Potent and selective inhibitors of an aspartyl protease-like endothelin converting enzyme identified in rat lung." <u>J. Med. Chem.</u> , 36(4):468-478, 1993  |
| D17 |  |
| D18 |  |

EXAMINER

DATE CONSIDERED

\* EXAMINER Initial if reference considered, whether or not citation is in conformance with MPEP 609: Draw line through citation if not in conformation and not considered. Include a copy of this form with the next communication to applicant.